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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,625	02/11/2002	Joseph R. Lakowicz	70089.0003USU1	4325
23552 7590 08/30/2007 MERCHANT & GOULD PC P.O. BOX 2903 MINNEAPOLIS, MN 55402-0903			EXAMINER STAPLES, MARK	
			ART UNIT 1637	PAPER NUMBER
			MAIL DATE 08/30/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/073,625

Applicant(s)

LAKOWICZ, JOSEPH R.

Examiner

Mark Staples

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28-43, 45-56, 59, 61-67 and 70-82 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28-43, 45-56, 59, 61-67 and 70-82 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicants' cancellation of claims 44 and 57 in the paper filed on 03/30/2007 is acknowledged.

Claims 28-43, 45-56, 59, 61-67, and 70-82 are pending and at issue.

Applicants' arguments filed on 03/30/2007 have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Withdrawn / Moot

2. The objections to the claims 44 and 57 are moot is withdrawn in light of the Applicant's cancellation of these claims.

Claim Rejections Withdrawn - 35 USC § 102(b) and 35 USC § 103(a)

3. Applicant's arguments, see pages 8-12, filed 03/30/2007, with respect to the rejection(s) of claim(s) 28-43, 45-56, 59, 61-67, and 70-82 under 35 USC § 102(b) and 35 USC § 103(a) have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, new grounds of

rejection are made in view of the new claim amendments. Please see new rejections which follow.

New Rejections Necessitated by Amendment

New Claim Rejections - 35 USC § 102(b)

4. Claims 28-43, 45-52, 59, 61-67, and 70-82 are rejected under 35 U.S.C. 102(b) as being anticipated by Natan et al. (United States Patent 6,149,868 filed October 28, 1998).

Regarding claims 28, 41, 46, 47, 61-63, 67, 70, 73, 74, and 77, Natan et al. teach a system and composition which is a nanometer scale structure (see claim 1) comprising a test sample and one or more metal particles arranged on a solid support which is SER-Active substrate (see Figure 1 and claim 1), wherein said test sample comprises one or more biomolecules (also see Figure 1 and claim 1), and wherein said one or more metal nanoparticles, a type of metal particle (also see Figure 1 and claim 1) and at least one of said one or more biomolecules in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation, through enhanced Raman scattering (see Abstract and entire patent), wherein an extrinsic fluorescent marker is not a part of the system, and wherein each of said one or more biomolecules is individually a biomolecule selected from the group consisting of a peptide (see claim 26), a protein (see Abstract), and a lipid (see

claim 26). Natan et al. teach where the system comprises colloidal metal nanoparticles (see 1st sentence of Abstract) which can be gold and/or silver (see claims 13-16).

Regarding claim 29, Natan et al. teach a system using borosilicate glass (see column 8, line 14).

Regarding claims 30 and 31, Natan et al. teach a system where the particles are in discontinuous films that is in an array of islands, and continuous films (see claim 7 and throughout the specification).

Regarding claims 32, 33, 48, 49, 75, and 76, Natan et al. teach metal nanoparticles coated with a film which is a polymer, a biopolymer, or a mixture of polymers and/or biopolymers or a metal oxide (see claims 20, 22, and 23).

Regarding claims 34-36, 52, 59, 73, 80, and 81 Natan et al. teach where two biomolecules can be attached to the nanoparticle, the first being a film which can be a polypeptide, an oligonucleotide, or a lipid (see claims 20 and 21) and the second of which is the analyte (see claim 1) which can be a protein (see Abstract). Natan et al. teach that biomolecules, especially proteins/polypeptides, have their intrinsic emission radiation affected (entire patent, especially the Abstract and the Figures).

Regarding claims 37 and 38, Natan et al. teach where the particle comprises noble metals of gold and/or silver (see claims 13-16).

Regarding claims 39, 50, and 71, Natan et al. teach 12 nm nanoparticles (see Figure1) which are sub-wavelength since the wavelength of radio waves is greater than 0.3 meters (as evidenced by Table 1 found at <http://science.jrank.org/pages/2368/Electromagnetic-Spectrum.html>).

Regarding claims 40, 51, and 72, Natan et al. teach where a distance between the metal nanoparticle surface and the metal substrate surface is between 1 and 50 nanometers, 10 to 500 angstroms (see claim 1), which overlaps the range of 50 to 200 angstroms.

Regarding claims 42, 43, 64, 65, 78, and 79, Natan et al. teach electromagnetic radiation at a wavelength of 400 nm which is about 295 nm (see column 13 line 12) and at a wavelength of 520.8 nm which is about 520 nm (see Figure 17A and its description under Brief Description of the Drawings).

Regarding claims 45, 66, and 82, Natan et al. teach multi-photon excitation by teaching both incoming and scattered photons (two types of photons; thus multi-photon, see column 18 lines 24 and 25).

New Claim Rejections - 35 USC § 103(a)

5. Claims 46-56, 59, 62-67, and 71-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. as applied to claims 46 and 67 above, and further in view of Lakowicz et al. (WO 99/36779, issued July 22, 1999).

Natan et al. teach as noted above.

Regarding claims 53-56, Natan et al. do not specifically teach where a biomolecule is labeled with an extrinsic fluorescent marker which can be a fluorophore.

Regarding claims 53-56, Lakowicz et al. teach that fluorophores can be conjugated to biological macromolecules including albumin (see page 23 line 34 continuing to page 24 and Example 1 following).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the biomolecules of Natan et al. by labeling them with fluorophores as suggested by Lakowicz et al. with a reasonable expectation of success. The motivation to do so is provided by Lakowicz et al. who teach: "These complexes [osmium (II) polypyridine fluorophores] can be used as red fluorophores for macromolecules. When using these fluorophores, one can avoid low signal to noise level by using gated observation. Another advantage of these compounds is high photostability. These dyes can be handled in room light for months" (see page 23 line 34 continuing to page 24). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Lakowicz et al. also disclose an assay in which a metal-ligand complex is used to bring into interactive proximity with the sample containing the analyte of interest. The mixture is irradiated with electromagnetic light energy to emit the light, which indicates the analyte of interest (See the Abstract and pg. 6, lines 16-24). The metal complexes are platinum metal, (See PG. 11, lines 19-20). The metal complex is a DPPG labeled vesicles (See pg. 12, lines 21-26). The metal-ligand complex is conjugated to human serum albumin (HSA) (See pg. 8, lines 6-8). The distance of the metal complex is 10 to 120 Å with the sample (See pg. 6, lines 16-24). Human serum albumin (HSA) is considered as a second biomolecule and is covalently linked to the metal (See column 21, lines 5-15). The ligand is carbon monoxide (See pg. 54, lines 17-21). The complex comprises of mono, bis or tris (heteroleptic) complexes of Ru (ii) and Os(II) and carbon

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monoxide diimine complexes of Re(I) (See pg. 11, lines 23-26). These teachings suggest that the metal particle is coated with an oxide as recited in claim 49. Lakowicz et al. further disclose that the assay is used to quantify the analyte of interest in which a first binding partner and a second binding partner are added to the sample, the first binding partner competes with the analyte to binding to the second binding partner, the first or second binding partner is labeled with a metal- ligand complex and the other is labeled with a photoluminescent energy transfer acceptor wherein the metal-ligand complex and photoluminescent energy transfer acceptor are chosen, when the first binding partner binds to the second binding partner, the metal-ligand complex and the photoluminescent energy transfer acceptor are brought in interactive proximity, producing a detectable change in luminescence (See pg. 53, lines 6-21). The metal-ligand complex typically absorb above 550 nm (See pg. 22, lines 20-22).

Conclusion

6. No claim is free of the prior art.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples *MS*
Examiner
Art Unit 1637
August 23, 2007

Kenneth R. Horlick
KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

8/28/07